

AMENDED CLAIMS

1. A method for obtaining a singular cell model capable of reproducing *in vitro* the metabolic idiosyncrasy of humans, wherein said model comprises a set of recombinant
5 adenoviral expression vectors that confer to the transformed cells a phenotypic profile of drug biotransformation enzymes designed at will, in order to reproduce the metabolic idiosyncrasy of humans, comprising:
- a) Transforming human cells of hepatic origin expressing reductase activity with a set of more than one recombinant adenoviral expression vectors comprising
10 ectopic DNA sequence that code for drug biotransformation enzymes selected from among Phase I drug biotransformation enzyme and Phase II drug biotransformation enzyme,
- wherein each expression vector comprises an ectopic DNA sequence that codes for a different Phase I or Phase II drug biotransformation enzyme,
15 selected from among:
- (i) a DNA sequence transcribed in the sense mRNA of a Phase I or Phase II drug biotransformation enzyme ("sense vector"); and
- (ii) a DNA sequence transcribed in the anti-sense mRNA of a Phase I or Phase II drug biotransformation enzyme ("anti-sense vector");
- 20 wherein the expression of said ectopic DNA sequences in the cells transformed with one or more of the aforementioned expression vectors confers the transformed cells specific phenotypic profiles of Phase I or Phase II drug biotransformation enzymes,
- to obtain with said expression vectors cells that transitorily express said ectopic
25 DNA sequences and present a different phenotypic profile of Phase I or Phase II drug biotransformation enzymes, and
- b) building a singular cell model capable of reproducing *in vitro* the metabolic idiosyncrasy of humans from said cells transformed with the aforementioned set of expression vectors, both sense and anti-sense vectors, so that the result is

the expression of any phenotypic profile of Phase I or Phase II drug biotransformation enzymes desired.

5 2. Method according to claim 1, wherein said Phase I and Phase II drug biotransformation enzymes are selected from among oxygenases, oxydases, hydrolases and conjugation enzymes.

10 3. Method according to claim 1, wherein said Phase I and Phase II drug biotransformation enzymes are selected from among monooxygenases dependent on CYP450, flavin-monooxygenases, sulfo-transferases, UDP-glucoronyl transferase, epoxide hydrolase and glutation transferase.

15 4. Method according to claim 1, wherein said ectopic DNA sequence coding for a Phase I or Phase II drug biotransformation enzyme is selected from among the group of DNA sequences transcribed in the sense mRNA or anti-sense mRNA of CYP450 isoenzymes and DNA sequences transcribed in the sense mRNA or anti-sense mRNA of oxygenases, oxidases, hydrolases and conjugation enzymes involved in drug biotransformation.

20 5. Method according to claim 1, wherein said ectopic DNA sequence coding for a Phase I or Phase II drug biotransformation enzyme is selected from among the group of DNA sequences transcribed in the sense mRNA or anti-sense mRNA of CYP 1A1, CYP 1A2, CYP 2A6, CYP 2B6, CYP 2C8, CYP 2C9, CYP 2C18, CYP 2C19, CYP 2D6, CYP 2E1, CYP 3A4, CYP 3A5, GST(A1), and DNA sequences
25 transcribed in the sense mRNA or anti-sense mRNA of flavin-monooxygenases, sulfo-transferases, UDP-glucoronyl transferase, epoxide hydrolase or glutation transferase.

30 6. Method according to claim 1, wherein said ectopic DNA sequence coding for a Phase I or Phase II drug biotransformation enzyme is a DNA sequence transcribed in the sense mRNA of a Phase I or Phase II drug biotransformation enzyme.

7. Method according to claim 1, wherein said ectopic DNA sequence coding for a Phase I or Phase II drug biotransformation enzyme is a DNA sequence transcribed in the anti-sense mRNA of a Phase I or Phase II drug biotransformation enzyme.
- 5
8. Method according to claim 1, which comprises the combined use of variable amounts of said expression vectors comprising ectopic DNA sequences coding for the drug biotransformation enzymes selected from among Phase I drug biotransformation enzymes and Phase II drug biotransformation enzymes.
- 10
9. A human cell model obtainable by a method according to any of claims 1-8.
- 15
10. Use of more than one sense or anti-sense recombinant adenoviral expression vectors comprising ectopic DNA sequence that code for different Phase I or Phase II drug biotransformation enzymes in the manipulation of cells expressing reductase activity to reproduce in them the metabolic variability found in humans.
- 20
11. A method for studying the metabolism and/or pharmacokinetics and/or potential idiosyncratic hepatotoxicity and/or potential medicament interactions of a drug, which comprises placing said drug in contact with a singular cell model capable of reproducing *in vitro* the metabolic idiosyncrasy of humans obtained according to the method of any of claims 1 to 8.
- 25
12. A kit comprised of more than one recombinant adenoviral expression vectors coding each for a different sense and anti-sense mRNA of the Phase I and Phase II drug biotransformation enzymes.
- 30
13. A method to confer to any cell line the capacity to metabolize xenobiotics in a controllable manner by means of an adenoviral set of more than one expression vectors of Phase I and Phase II enzymes, as well as of cytochrome P450 reductase, comprising the transfection of said cell type with said adenoviral

- 5 expression vectors in order to confer to the transformed cells a phenotypic profile designed at will, up to metabolize xenobiotics characterised in that the transformation of a cell type expressing cytochrome P450 reductase activity is carried out with a set of more than one expression vectors comprising ectopic DNA sequences coding P450 enzymes involved in the xenobiotic biotransformation, wherein each expression vector comprises an ectopic DNA sequence transcribing for the sense mRNA of a different CYP enzyme, wherein the expression of all of said ectopic sequences in the transformed cells confers to them a transitory xenobiotic metabolic profile.